REMARKS

Reconsideration of the present Application in view of the above amendments and following remarks is respectfully requested. Applicants have cancelled claim 3 without acquiescence to any rejection and without prejudice to the filing of any related divisional, continuation, or continuation-in-part application. Applicants have amended claims 1, 5-7, 23, and 24 to more clearly describe an embodiment of Applicants' invention. Support for the amended claims may be found in the application as originally filed, for example, at page 40, line 26 through page 41, line 18; page 45, line 17 through page 46, line 7; page 50, line 22 through page 54, line 2; SEQ ID NOs:1, 2, 3, 12, and 13. No new matter has been added.

COMPLIANCE WITH SEQUENCE RULES

The PTO asserts that the Application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. Specifically, the PTO asserts that amino acid sequences presented in Figure 3 that correspond to transmembrane domains are not provided in the sequence listing. The PTO also asserts that the specification needs to be amended to comply with 37 C.F.R. § 1.821(d) to provide a reference to a particular sequence identifier for a sequence that is referred to in the specification or the claims. The PTO also requests that sequence identifiers corresponding to the five amino acid sequences presented in Figure 4 be provided.

Applicants thank the PTO for pointing out these informalities in the Application. As requested by the PTO, Applicants have enclosed electronic and paper copies of an updated Sequence Listing, which include the amino acid sequences corresponding to transmembrane domains as shown in Figure 3, but which include no new matter that goes beyond the original Application as filed. Furthermore, these amendments, which merely direct the insertion of the Sequence Listing and insertion of sequence identifiers, include no matter that goes beyond the original Application as filed.

Applicants also submit that in view of the Amendments to the Brief Description of the Drawings submitted herewith, specifically to include sequence identifiers for the sequences presented in Figures 3 and 4, the specification is in compliance with the sequence rules. Applicants respectfully submit that the Amendments introduce no new matter into the

Application. Accordingly, the Application is in compliance with 37 C.F.R. §§ 1.821-1.825 and WIPO Standard ST. 25 and Applicants respectfully request that the objections be withdrawn.

OBJECTION TO THE SPECIFICATION

The PTO objects to the disclosure, asserting that the specification contains an embedded hyperlink or other form of browser-executable code, for example, at page 96, line 23. The PTO also asserts that trademarks such as the marks that appear on page 62, line 20, should be capitalized and accompanied by the generic terminology.

Applicants respectfully submit that to conform to the Internet citation format provided in M.P.E.P. § 707.05(e), the specification has been amended by replacing paragraphs with redlined paragraphs at page 16, line 21; page 29, line 26; page 30, line 10; page 88, line 6; and page 96, line 7. Applicants have also amended the paragraph beginning on page 62, line 13 to include the generic names for the compositions with registered trademarks. Applicants respectfully submit that the Amendments to the specification submitted herewith obviate the objections to the specification, and respectfully request that the objections be withdrawn.

The PTO also asserts that Tables 1 and 3 are identical and Tables 2 and 4 are identical and therefore duplicative. The Examiner suggests that the second copy of each table be deleted and a substitute specification be submitted.

Applicants respectfully submit that Tables 1 and 2 illustrate data related to one clone of the invention ABCG4 polynucleotide, and Tables 3 and 4 present data related to a second clone of the ABCG4 polynucleotide. Applicants further submit that presentation of the data in two different examples and in tables with different titles, column headings, and row headings clearly points out that the data were obtained from independent analyses. Accordingly, Applicants respectfully request that Tables 1-4 be retained in the instant specification and request that the objection be withdrawn.

OBJECTION TO THE CLAIMS UNDER 37 C.F.R. § 1.75(C)

The PTO objects to claim 3 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of claim 1. Specifically, the Action asserts that a proper dependent claim cannot be infringed by anything that would not infringe the independent claim on which it depends, and allegedly, the subject invention nucleic acid molecule of claim 3 can be infringed by a nucleic acid molecule that does not infringe claim 1.

Applicants respectfully submit that the Amendments submitted herewith, which include amendments to claim 1 and cancellation of claim 3, obviate the basis for this objection. Accordingly, Applicants respectfully request that the objection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The PTO rejects claims 1 and 3-8 under 35 U.S.C. § 112, first paragraph, asserting that the claims are directed to subject matter that is not adequately described in the specification. In particular, the PTO alleges that the specification fails to describe the genus of nucleic acids that encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2 or 13. The PTO further asserts that neither the claimed species nor genus is described by sufficient relevant identifying characteristics to convey to a person skilled in the art that Applicants possessed the claimed genus of nucleic acid molecules at the time the Application was filed.

Applicants respectfully traverse the grounds for this rejection and submit that, as disclosed in the specification and recited in the instant claims, Applicants possessed the claimed invention at the time the Application was filed. Applicants' invention is directed in pertinent part to an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide, which comprises the amino acid sequence set forth in SEQ ID NO: 2 or 13, or the complement of such a nucleotide sequence, and to related compositions and methods.

Applicants respectfully submit that the present specification provides sufficient, relevant, identifying characteristics of the claimed polynucleotides. Applicants have disclosed the nucleotide sequence of nucleic acid molecules (*see* SEQ ID NO: 1, 3, and 12) that encode a

novel, full-length ABCG4 polypeptide (*see* SEQ ID NOs:2 and 13). Furthermore, sufficient, relevant, identifying characteristics of an allelic variant of an ABCG4 polypeptide are described in detail in the instant specification, for example, at page 19, lines 7-26 and at page 20, line 4 through page 21, line 13. Nevertheless, solely to expedite prosecution of this matter without acquiescence to this rejection, Applicants have amended claim 1, obviating the basis for this rejection.

Accordingly, Applicants respectfully submit that the specification reasonably conveys to a person skilled in the art that Applicants possessed the claimed invention at the time the Application was filed. Applicants therefore respectfully submit that the claimed subject matter is adequately described by the specification in compliance with the written description requirement under 35 U.S.C. § 112, first paragraph, and request that these rejections be withdrawn.

REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH (ENABLEMENT)

Claims 23 and 24 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Specifically, the PTO asserts that undue experimentation would be required to determine what is the "pharmaceutically effective amount" of a composition comprising the nucleic acid molecule of SEQ ID NO:1 or 12 or of a composition comprising an antisense oligonucleotide that is capable of hybridizing to SEQ ID NO:1 or 12.

Applicants respectfully traverse this rejection and submit that as disclosed in the present specification and recited in the instant claims, Applicants fully enabled the claimed invention at the time the Application was filed. Applicants submit that the instant specification provides explicit guidance enabling a person skilled in the art to make and use, readily and without undue experimentation, a composition comprising a nucleic acid molecule that comprises a nucleotide sequence set forth in SEQ ID NO:1, 3, or 12 and a suitable carrier; and to a composition comprising (1) an antisense nucleic acid molecule that comprises a nucleotide sequence that is complementary to (a) a sequence encoding a polypeptide, which polypeptide

comprises an amino acid sequence set forth in SEQ ID NO:2 or 13, or (b) a sequence set forth in SEQ ID NO: 1, 3, or 12; and (2) a suitable carrier.

Given the teachings of the instant specification, a person skilled in the art can identify an isolated polynucleotide having a nucleotide sequence (SEQ ID NO: 1, 3, or 12) that encodes an ABCG4 transporter polypeptide (SEQ ID NO: 2 or 13) or that has a sequence that is complementary to such a nucleotide sequence (*see, e.g.,* page 15, line 3 through page 16, line 21; Sequence Listing). The specification also explicitly describes how to make and use an antisense nucleic acid molecule that has a sequence complementary to the coding region of a double-stranded DNA or an mRNA sequence that encodes a ABCG4 polypeptide or that includes 5' and 3' noncoding regions of SEQ ID NO:1 or SEQ ID NO: 12 that flank the coding region (*see, e.g.,* page 16, lines 6-13; page 22, line 19 through page 23, line 5; SEQ ID NO: 1, and 12; *see generally* page 22, line 19 through page 25, line 18). In addition, persons skilled in the art can select a suitable carrier that may be acceptable for administration to a subject, for example, on the basis of suitability for a proposed route of administration, stability of the active compound, and storage requirements (*see generally* page 50, line 22 through page 55, line 13). Such carriers are well known in the art and described in the present specification (*see, e.g.,* page 50, line 22 through page 54, line 11). The amount of a nucleic acid molecule comprising SEQ ID NO:1, 3, or 12, or the amount of an antisense nucleic acid molecule as recited included in the claimed compositions depends upon the intended use of such compositions. By way of example, if the claimed composition is to be used in an animal model, the quantity of the nucleic acid molecule may be readily determined without undue experimentation according to methods for evaluating toxicity and therapeutic efficacy that are well known in the art and described in the specification (*see, e.g.,* page 54, line 3 through page 55, line 13). *See also Ex parte Skuballa*, 12 U.S.P.Q.2d 1570, 1571 (Bd. Pat. App. & Int. 1989) (finding that a skilled worker in the art could readily optimize effective dosages and administration regimens according to simple routine procedures).

Thus, Applicants submit that the specification provides enabling disclosure for a skilled artisan to make and use the claimed compositions readily and without undue experimentation. Accordingly, Applicants respectfully submit that the requirements for

enablement under 35 U.S.C. § 112, first paragraph, are met and request that this rejection of the claims be withdrawn.

REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-8 and 24 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. In particular, the PTO asserts that the metes and bounds of the limitation "selectively binds" in claim 1 cannot be determined, rendering the claim vague and indefinite. The PTO alleges that claim 6 is vague and indefinite because it depends from itself. For examination, the Examiner interprets claim 6 to be dependent from claim 5. Claim 24 also stands rejected for indefiniteness for recitation of the term "specifically hybridizing." The PTO rejects claims 2-5, 7, and 8 as indefinite because they depend from an allegedly indefinite claim.

Applicants respectfully traverse these grounds for rejection and submit that the instant claims particularly point out and distinctly claim what Applicants regard as their invention. Applicants respectfully submit that in view of the Amendments submitted herewith, which includes amendments to claims 1, 6, and 24 and cancellation of claim 3, the basis for rejection of these claims has been obviated.

Amended claim 1 is directed in pertinent part to an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide that comprises the amino acid sequence set forth in SEQ ID NO: 2 or 13, or that comprises the complement of the nucleotide sequence. Present claim 24 is directed to a composition comprising (1) an antisense nucleic acid molecule that comprises a nucleotide sequence that is complementary to (a) a sequence encoding a polypeptide, which polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 2 or 13, or (b) a sequence set forth in SEQ ID NO: 1, 3, or 12; and (2) a suitable carrier. Applicants thank the Examiner for pointing out the typographical error in claim 6, which Applicants have amended to recite proper dependency on claim 5. Applicants further submit that dependent claims 2, 4, 5, 7, and 8 depend from definite claims and thus are definite.

In view of the present amendment and the above remarks, Applicants respectfully submit that the instant claims meet the requirements for definiteness under 35 U.S.C. § 112, second paragraph. Applicants therefore request that the rejection of these claims be withdrawn.

Applicants respectfully submit that all claims remaining in the Application are believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at (206) 622-4900.

Respectfully submitted,

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Enclosures:

Sequence Listing
CRF of Sequence Listing on CD
Declaration Regarding Sequence Listing

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